

Emergency treatment and prevention of insect-sting anaphylaxis

Sunday Clark and Carlos A. Camargo Jr

Purpose of review

Hymenoptera stings are thought to cause systemic allergic reactions in 0.4–5% of individuals, and to account for 40–100 deaths annually in the USA. This review examines current research on insect-sting anaphylaxis in the emergency department (ED), and provides suggestions on how to improve ED treatment and prevention.

Recent findings

Few published studies since January 2005 examine the emergency management of insect-sting allergic reactions. Earlier studies found that few ED patients with this problem received health education, a prescription for self-injectable epinephrine or referral to an allergy specialist at ED discharge. A recent multicenter study by our group demonstrated that ED patients with insect-sting allergic reactions continue to receive care discordant with national guidelines for the emergency management of anaphylaxis.

Summary

Concordance with national guidelines for the treatment of anaphylaxis remains poor among insect-sting allergy patients. The development of a simple, clinical definition of anaphylaxis is urgently needed to facilitate identification of cases. Such a definition would help tremendously with dissemination of emergency management guidelines and the creation of systems for their implementation. All of these steps are essential for the improved treatment and prevention of insect-sting anaphylaxis in the ED.

Keywords

anaphylaxis, emergency department, insect stings

Introduction

The lifetime prevalence of anaphylaxis in Westernized countries has been very difficult to determine. A literature review by Neugut and colleagues [1] estimated the US incidence of anaphylaxis to be anywhere between 1 and 15%. By contrast, a population-based study in Olmsted County, Minnesota, by Yocum and colleagues [2] concluded that the prevalence of anaphylaxis was less than 1%. A review of recent studies from the USA, Canada and the UK yields prevalence estimates ranging from 0.3–0.6 to 0.95% [3–6].

Many of these allergic reactions are managed in the emergency department (ED). For example, a managed care study from Washington State estimated that 71% of all anaphylaxis reactions in a healthcare system were seen in the ED [3]. Nevertheless, the prevalence of anaphylaxis among all ED visits is less than 1% [7,8], or approximately 400 000 visits/year (unpublished data). Among this relatively large group of ED patients, anywhere from 1.4 to 59% of acute allergic reactions are due to insect stings [9–11]. This uncertainty is not surprising given the diverse estimates of the percentage of all anaphylaxis due to insect stings – regardless of clinical setting. For example, Hymenoptera stings (e.g. fire ants, wasps, yellow jackets and hornets) are thought to have caused anaphylaxis, at some point, in 0.4–5% of the general population [1,12–14]. Other studies [15–19] report that systemic allergic reactions to Hymenoptera venom occur in 0.4–3.3% of individuals. Looking beyond lifetime prevalence and percentage of ED visits, vital statistics suggest that approximately 40–100 Americans die every year as a result of insect stings [20,21]. Even these numbers are thought to be inaccurate, however, with most experts convinced that they are gross underestimates [1,13,14,22,23].

Regardless of the exact numbers, patients continue to visit EDs for management of insect-sting-related allergic reactions. Timely and appropriate treatment is necessary to prevent progression of the allergic reaction. Moreover, there is a growing emphasis on education and preventive measures, as individuals with a history of anaphylaxis are at an increased risk of a subsequent episode [22]. To that end, national guidelines recommend treatment of all severe allergic and anaphylactic reactions with epinephrine, teaching of proper techniques for self-injectable epinephrine and referral to an allergist for further care [2,22,24,25].

Curr Opin Allergy Clin Immunol 6:279–283. © 2006 Lippincott Williams & Wilkins.

Department of Emergency Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA

Correspondence to Sunday Clark MPH, ScD, EMNet Coordinating Center, Department of Emergency Medicine, Massachusetts General Hospital, 326 Cambridge Street, Suite 410, Boston, MA 02114, USA
Tel: +1 617 724 0304; fax: +1 617 724 4050; e-mail: sclark3@partners.org

Current Opinion in Allergy and Clinical Immunology 2006, 6:279–283

Abbreviation

ED emergency department

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1528-4050

A prompt and accurate diagnosis identifies those at greatest risk for adverse outcomes. An accurate diagnosis is, of course, essential for effective emergency management [26]. Given such large variability in current anaphylaxis estimates in the general population and in the ED – and studies suggesting that the prevalence of allergies is rising [1,10] – there truly is an urgent need to develop clinical definitions that assist in diagnosis. Such a tool would allow better measurement of the actual prevalence of all types of anaphylaxis and promote improved ED treatment. Correct patient identification also could be used to target prevention efforts among those individuals at highest risk of a recurrent insect sting.

This article reviews the sparse literature on the treatment and prevention of insect-sting related anaphylaxis in the ED. Additionally, we suggest steps that can be taken to improve the identification and overall management of this condition in the ED setting.

Assessment of emergency department management

Unfortunately, there are few published studies since January 2005 on the emergency management of insect-sting-related anaphylaxis. Earlier publications assessed emergency management of allergic reactions in general (including anaphylaxis) and, in a few studies, authors described the treatment of insect-sting-related reactions within their allergy cohorts. For example, a 1996 British study by Stewart and Ewan [27] found that among eight patients with severe allergic reactions to known causes, three (38%) were caused by an insect sting. None of these anaphylaxis patients was given advice about avoidance of the offending allergen, prescribed self-injectable epinephrine or referred directly to an allergy specialist. Among another 13 patients with less severe generalized reactions and a known cause, three (23%) were caused by insect stings (wasps). During a second survey conducted during peak bee and wasp season, eight (89%) of nine anaphylaxis cases were due to bee or wasp stings. In this second group, three (38%) of the eight were treated with adrenaline. While no patients were given a prescription for self-injectable epinephrine in the ED, five (63%) were referred to an allergy clinic.

In 2001, Brown and McKinnon [28] described the clinical features, management and outcomes of anaphylaxis in a single Australian ED. Among the 162 patients with acute allergic reactions, 57% had a known causative agent, while among the 142 patients with anaphylaxis, 73% had a known causative agent. In the anaphylaxis group, 18% of cases were due to insect stings (eight wasp, two tick, one ant, one bee, 12 unknown). Among all patients treated in the ED, 18% received adrenaline before arrival and an additional 27% received adrenaline while in the ED (i.e. total of 45% received epinephrine for their

anaphylaxis in this single ED). Seven (5%) patients were given replacement self-injectable epinephrine and 47 (35%) were referred to follow-up care: 23% to an allergy clinic, 2% to medical outpatient clinic and 10% to their local physician.

In 2003, Bellou and colleagues [10] reviewed the charts of 324 patients in France presenting to the ED for an allergic event and found that 78 (24%) patients were diagnosed with insect-sting allergy. Three (4%) of the insect-sting-allergy patients were observed to have anaphylactic shock. While in the ED, 10 (3%) of the patients received epinephrine. Among the 233 discharged patients seen in the ED for an allergic event, 55 (24%) were referred by an emergency physician for an 'allergy consultation'. Among these patients, 28 patients were referred directly to an allergy unit and four were referred to an allergist.

Around the same time, Helbling and colleagues [11] evaluated the incidence and causes of severe anaphylactic reactions in Switzerland. Among 7739 medical records reviewed over the 3-year period, 215 (2.8%) were determined to have anaphylaxis. Insect stings were documented as the cause of the anaphylactic reaction in 133 (59%) of the cases. Among all 215 patients with anaphylaxis, 210 (98%) required emergency medical assistance. Almost 50% of the anaphylaxis cases were treated with epinephrine in the ED. No information was provided regarding ED discharge plans.

A recent multicenter study by our group [29^{••}], the Emergency Medicine Network (www.emnet-usa.org), reviewed the ED charts of 617 patients identified by the ICD-9 code and chart review as having an insect-sting-related allergic reaction in the USA. Among these ED patients, from 15 North American EDs, 358 (58%) had local reactions and 259 (42%) had systemic reactions. We further characterized patients with systemic reactions according to severity classifications proposed by Brown [30]. Among the 259 patients with systemic reactions, 70 (27%) had mild systemic reactions, 143 (55%) had moderate reactions and 46 (18%) had severe reactions. Overall, 6% of the patients received epinephrine in the ED and among patients categorized as having anaphylaxis, this number only rose to 13%. Among patients with systemic reactions, 15% were documented as having received instructions to avoid the offending allergen. A prescription for self-injectable epinephrine only was documented for 27% of patients. Additionally, only 20% had documentation of referral to an allergy specialist.

Among the original group of 617 ED patients with insect-sting allergic reactions, 31% were identified as having a *severe* insect-sting-related allergic reaction [29^{••}]. The severe life-threatening reactions were determined based on patients' documented signs and symptoms at ED

presentation or during the ED course. A severe allergic reaction or 'anaphylaxis' was defined as the involvement of two or more organ systems from the following: skin (e.g. hives), respiratory (e.g. trouble breathing or shortness of breath; stridor, wheezing), cardiovascular (e.g. hypotension, dizziness or fainting, altered mental status) and gastrointestinal (e.g. abdominal pain). The presence of hypotension, defined as a systolic blood pressure of less than 100 mmHg, automatically led to classification as anaphylaxis. Even among patients considered to have anaphylaxis, concordance with recommended guidelines for the emergency management of anaphylaxis was low. In this subset, only 13% of patients received epinephrine in the ED, 31% had documentation of a discharge prescription for self-injectable epinephrine and 21% had documentation of referral to an allergist.

Requirements for improved emergency department management and implementing new systems

The initial step needed to begin improvement of the emergency management of insect-sting-related anaphylaxis is for anaphylaxis experts to develop and validate a clear, clinical definition for anaphylaxis. Two recent multidisciplinary conferences [31^{••},32^{••}], in April 2004 and July 2005, sought to develop such a definition. Both conferences were co-sponsored by the National Institutes of Health and the Food Allergy and Anaphylaxis Network and included emergency physicians. Given the complexity of anaphylaxis and its myriad presentations, the group acknowledged that experts in allergy/immunology probably would benefit least from these clinical criteria – but that was not the motivation behind their development. The criteria were written to assist *nonspecialists* to better identify individuals with anaphylaxis and then, having identified cases, to encourage improved treatment of anaphylaxis.

For patients with an acute-onset illness, two organ systems should be involved, including skin/mucosal tissue and either airway compromise or reduced blood pressure. Alternatively, anaphylaxis is likely if a patient has exposure to a known allergen, symptoms develop within minutes to hours of exposure and two of the following criteria are met: a history of anaphylaxis, involvement of skin/mucosal tissue, airway compromise, reduced blood pressure or persistent gastrointestinal symptoms (e.g. crampy abdominal pain, vomiting). Finally, exposure to a known allergen and the presence of hypotension should raise concern about anaphylaxis. The conference attendees agreed that a patient seen in the ED for an acute allergic reaction who satisfies any one of these three separate clinical criteria probably has anaphylaxis.

While most allergic reactions, such as simple urticaria, can be managed successfully without epinephrine treatment,

clinicians should strive to quickly identify the more severe allergic reactions (anaphylaxis) that would benefit from intramuscular epinephrine. Although cutaneous symptoms are extremely common for insect-sting allergic reactions, a wide array of clinical signs and symptoms may be present as a result of the generalized reaction [30,33]. A unique challenge for insect stings is the distinction between local reactions and true systemic reactions. Large local reactions also can be mistakenly diagnosed as cellulitis [19]. In our experience, the stages between a local reaction and systemic reaction (including anaphylaxis) [34] are not widely appreciated by nonallergists. These concepts merit greater emphasis in future efforts to teach about insect-sting-related allergic reactions to ED staff.

While a simple, symptom-based approach to identifying anaphylaxis can be useful for clinical management and for research purposes, it also must be rigorously tested against expert judgment. Evaluating the definition against actual diagnosis made by emergency physicians (without the benefit of the tool) and the expert opinion of trained allergists (the criterion standard) will allow a better understanding of the test characteristics of this definition. For example, what percentage of actual anaphylaxis patients does it identify as having anaphylaxis (i.e. sensitivity)? Future studies also will need to identify whether the suggested criteria should be refined before implementation on a national scale.

With or without the new clinical criteria, clinicians need to promptly initiate therapy after reaching a diagnosis of anaphylaxis. Once in the ED, suggested therapy includes administration of intramuscular epinephrine [19,33,35]. Consensus guidelines were put forth by the Project Team of the Resuscitation Council (UK) in 2001 for the treatment of anaphylaxis by medical first-responders [36]. These consensus guidelines include a schema for the identification of an anaphylactic reaction and the progression of treatment based on the continuation or resolution of symptoms. Treatment by first responders included oxygen treatment and epinephrine (1:1000 solution, 0.5 ml [500 µg] intramuscularly). Repeat epinephrine and antihistamine (10–20 mg intramuscularly or slowly intravenously) treatment was recommended for patients whose symptoms did not resolve after initial treatment. Intramuscular or slow intravenous hydrocortisone (100–500 mg) and intravenous fluids (1–2 l intravenously) were recommended for patients who did not respond or progressed to clinical manifestations of shock.

An algorithm for the diagnosis and treatment of acute allergic reactions and anaphylaxis, including insect-sting-related reactions, may allow more prompt and more appropriate treatment. One approach to facilitating the

implementation of an emergency management algorithm (in the prehospital and hospital settings) would be to develop electronic diagnosis and order forms that prompt first responders and ED staff to assess signs and symptoms if an allergic reaction is suspected, and to initiate appropriate treatment. Electronic approaches also can be used to help prevent future reactions and to help patients manage future reactions if they do occur. For example, electronic tools can be used to advance three prevention strategies: education, a prescription for self-injectable epinephrine and referral to an allergy specialist. All three contribute to a successful plan after ED management [19].

Education of patients should include instructions for allergen avoidance, a written emergency action plan and a listing of educational resources. Instructions for how to avoid the offending insect in the future can include guidelines for wearing long pants and shirts when outside, avoiding pollinated plants and grassy areas, avoiding perfumes and fragrant soaps and lotions, and avoiding eating and drinking outdoors, especially from straws or cans that could harbor an insect.

A prescription for self-injectable epinephrine will allow individuals with a history of a severe allergic or anaphylactic reaction to be prepared for prompt treatment if another exposure occurs. Self-injectable epinephrine can be important for the treatment of future insect-sting-related allergic reactions, as well as for a biphasic reaction. Biphasic reactions are thought to comprise 5–20% of anaphylactic reactions [37,38]. While observation in the ED for 6–8 h, or even 24 h [33], may be ideal, this is not often practical in today's crowded EDs. The prescription (and filling of the prescription) for self-injectable epinephrine at ED discharge can be life-saving in the event of a biphasic reaction or a future anaphylactic reaction. In addition to writing the prescription and encouraging patients to fill the prescriptions, instructions for the appropriate use of a self-injectable epinephrine device should be given at the time at which the patient receives the prescription. It is important that patients are only discharged with a friend or family member who can be with the patient for several hours following discharge in the event that a biphasic reaction occurs [19].

Finally, anaphylaxis patients should be referred to an allergy specialist following an anaphylactic reaction treated in the ED. This referral will allow patients to receive a thorough evaluation, specialized follow-up care, more intensive education about allergic reactions and anaphylaxis, including guidance for early recognition of signs and symptoms of an allergic reaction, and evaluation for immunotherapy. Immunotherapy has been shown to be highly effective in preventing future reactions in patients with a history of anaphylaxis to venom [19,39].

A meta-analysis [39] including eight studies evaluating the effectiveness of venom immunotherapy found that 79% of patients who received specific immunotherapy had symptoms prevented upon venom re-exposure. For this reason, it is particularly important to arrange follow-up with an allergist following an ED visit for insect-sting-related anaphylaxis. Identification of these patients for referral would be greatly facilitated by general agreement on a single user-friendly definition.

Conclusion

Concordance with national guidelines for the treatment of anaphylaxis remains low – both overall and in the specific case of insect-sting-related anaphylaxis. The recent development of a simple, clinical definition to identify anaphylaxis is welcome, though it will require validation before widespread adoption and use. The development of an easy-to-follow electronic algorithm that allows for quick identification of symptoms suggesting anaphylaxis and then recommended treatment strategies (e.g. intramuscular epinephrine) may help to further improve the management of anaphylaxis in the ED. At discharge, key concepts include education, prescription for self-injectable epinephrine and referral to an allergist for venom immunotherapy. Over the past year, there has been definite progress toward these goals but more work is needed.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 304).

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